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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,755	03/09/2001	Seth A. Darst	IPT-012.01	8223

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EXAMINER
LY, CHEYNE D

ART UNIT	PAPER NUMBER
1631	18

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,755	DARST ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-26 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29 and 31-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' arguments in Paper No. 17, filed June 02, 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. The addition of new claims 31-47 has been acknowledged.

OBJECTIONS

3. The disclosure is objected to because of the following informalities:

4. Formal drawings, Paper 13, filed November 12, 2002, have figures that contain parts therein designated by capital letters such as 2A, 2B, etc, while lower case letters are utilized for figure part designations in the specification in the section entitled BRIEF DESCRIPTION OF THE DRAWINGS. Appropriate correction is required to resolve such conflicts. Applicants are encouraged to review the whole specification for such differences in figure designations because similar designation conflicts are present in the specification on page 58, line 25, and elsewhere.

IDS

5. Applicants' response is acknowledged and document EU (Arora, Molecular Pharmacology, Volume 23, pages 133-140, 1983) has been considered.

Sequence Compliance

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). See, for example, Figure 1, amino acid sequences; and Figure 6B, nucleic acid sequences. However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because Figure 1, contains amino acid sequences with sequence lengths that are equal to or greater than 4 amino acid molecules and these sequences do not have SEQ ID Nos cited along with each sequence in the specification or Figure; and Figure 6B, contains nucleic acid sequences with sequence lengths that are equal to or greater than 10 nucleic acid molecules and these sequences do not have SEQ ID Nos cited along with each sequence in the specification or Figure. Applicants are also reminded that SEQ ID Nos are not required in Figures per se, however, the corresponding SEQ ID Nos then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicant(s) are required to submit a new computer readable form sequence listing, a paper copy for the specification, statements under 37 CFR § 1.821(f) and (g), if there is a need to list additional sequences in the listing. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

NEW CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

7. Claims 33-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. This is a new matter rejection, which is necessitated by amendment.

9. Specific to claims 33-35, the limitation of "within at least approximately 10 A of the center of the position of the bound rifampicin as defined by the coordinates in Table 2" is not disclosed in the instant specification. It is acknowledged that Applicants disclose the closest approach of rifampicin...is 12.1 A (page 61, lines 4-6).

10. Specific to claims 36-47, the limitation of "backbone atoms of at least [three, five, or ten] amino acid residues selected from the group" is not disclosed in the instant specification regarding "the portion" utilized for performing rational drug design.

New Provisional Obvious-Type Double Patenting Rejection

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438,

164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

12. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

13. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 27-29 and 31-47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 8 of U. S. Patent No. US 6,225,076 B1 (Darst et al.) in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983).

15. This rejection is necessitated by Applicants amendments.

16. Claims 7 and 8 of U. S. Patent No. US 6,225,076 B1 (Darst et al.) claim a method of identifying an agent that inhibits bacterial growth comprising:

17. (a) selecting a potential agent by performing rational drug design with the set of atomic coordinates in Table 3, wherein said selecting is performed in conjunction with computer modeling;

18. (b) contacting the potential agent with a bacterial culture; and

19. (c) measuring the growth of the bacterial culture under conditions in which the bacterial culture grows in the absence of the agent; wherein a potential agent is identified as an agent

that inhibits bacterial growth when there is a decrease in the growth of the bacterial culture in the presence of the agent relative to in its absence.

20. (d) contacting the agent with a eukaryotic cell; and

21. (e) measuring the amount of proliferation of the eukaryotic cell under conditions in which the eukaryotic cell proliferates in the absence of the agent; wherein an agent is identified as an agent for inhibiting bacterial growth when there is no change in the proliferation of the eukaryotic cell in the presence of the agent relative to in its absence; and wherein the agent identified inhibits bacterial growth but not eukaryotic proliferation, as in instant claims 27-29 and 33-47. It is noted that the specific limitation of atomic coordinates in Table 2 of claim 27 and dependent claims; and the further limiting requirements of claims 33-47 are directed to nonfunctional descriptive material as discussed below.

22. Further, once the agent is identified, the said agent may be synthesized de novo (column 22, lines 28-29), as in instant claims 31 and 32. "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent" (MPEP § 804 (II) (B) (1)).

23. Even though the method disclosed by Darst et al. does not specify that the atomic coordinates be derived from rifampicin bound to the core RNA polymerase (Rif-RNAP), the specific limitations of atomic coordinates of rifampicin bound to the core RNA polymerase in this instant case do not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.

24. In re Gulack defines nonfunctional descriptive material, as when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in term of patentability. Also, the MPEP indicates that descriptive material that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition (MPEP § 2106 (IV)(B)(b)).

25. Darst et al. discloses, "[i]nitially, compounds known to bind bacterial RNA polymerase, for example rifampicin which binds to the .beta. subunit, can be systematically modified by computer modeling programs until one or more promising potential analogs are identified" (Column 22, lines 1-8). This is achieved by fitting of potential modulators such as rifampicin to the RNA polymerase by 3-D modeling based on crystal structure data thus suggests the crystal structure of rifampicin-bound RNA polymerase (column 21, lines 40-44).

26. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Darst et al. for a method of identifying a compound that is predicted to inhibit bacterial growth. Darst et al. also teaches compounds such as rifampicin which bind to RNA polymerase could be model to identify analogs (Column 22, lines 1-8) and "[a] potential inhibitor (e.g., a candidate drug) would be expected to interfere with bacterial growth" (Column 24, lines 52-55). Further, the critical limitation of atomic coordinates of rifampicin bound to the core RNA polymerase is regarded as nonfunctional descriptive material as defined by In re Gulack. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use

the method of Darst et al. for identifying a compound that is predicted to inhibit bacterial growth.

Response to Applicants' Arguments

27. Applicants argue that U. S. Patent No. US 6,225,076 B1 does not disclose or suggest that the crystal structure of rifampicin-bound RNA polymerase be determined and that certain of the resultant coordinates be used in a method for identifying bacterial growth inhibitors. Applicants cite *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991) and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985) to argue that an obvious-type double patenting rejection must follow fact pattern as 35 U.S.C. § 103 rejection. Further, all the claim limitations must be taught in the prior. Applicants' argument has been fully considered and found to be unpersuasive because "the specification can always be used as a dictionary to learn the meaning of a term in the patent claim. Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent" (MPEP § 804 (II) (B) (1)).

28. Specific to Applicants' argument that U. S. Patent No. US 6,225,076 B1 does not disclose or suggest that the crystal structure of rifampicin-bound RNA polymerase be determined and that certain of the resultant coordinates be used in a method for identifying bacterial growth inhibitors, it is noted that the specific limitation of defining the structure of rifampicin-bound RNA polymerase according to the atomic coordinates of Table 2 is directed to nonfunctional descriptive material as discussed above.

29. Specific to the argument Darst et al. does not suggest the crystal structure of rifampcin-bound RNA polymerase be determined. Darst et al. discloses of the fitting of potential modulators such as rifampicin to the RNA polymerase by 3-D modeling based on crystal structure data thus suggests the crystal structure of rifampicin-bound RNA polymerase (column 21, lines 40-44).

30. It is suggested that Applicants submit a Terminal Disclaimer to overcome the instant Provisional Obvious-Type Double Patenting rejection. (MPEP § 1490).

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

31. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

32. Claims 27-29 and 31-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal core RNA polymerase with rifampicin which have atom coordinates instantly disclosed, does not reasonably provide enablement for a crystal of a portion of the core RNA polymerase with rifampicin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

33. This rejection is maintained with respect to claims 27-29, as recited in the previous office action Paper No. 15, mailed January 29, 2003. The instant rejection is extended to claims 31-47.

34. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Response to Applicants' Arguments

35. Applicants argue that a new crystal of a portion of the Rif-RNAP is not required; therefore, the claimed invention commensurate in scope with these claims is enabled. Applicants' argument have fully considered and found to be unpersuasive due to the unpredictability of the art of protein crystallization.

36. The limitation of a portion of the Rif-RNAP structure of step (a) may be directed to a separately crystallized entity wherein defining it as a portion of Rif-RNAP occurs via the Table 2 coordinates is performed via the "sufficient structural information" limitation of claim 27, part (a). That is, protein segments bound to Rif would be sufficiently Rif-RNAP is sufficient correspondence, inclusive of less than total, was present to the coordinates of said Table 2.

37. It is further noted that limitation of "defining the structure of rifampicin... or a portion of the Rif-RNAP by the atomic coordinates in Table 2" depends from data that have been generated from protein crystallization. As cited in Paper No. 15, it is well known in the art that the protein crystallization process has been characterized as a "trial-and-error" process at best; therefore, the data generated from such process is regarded as unpredictable. Due to the unpredictability of said data such as atomic coordinates in Table 2, one of skill in the art would not be able to define crystals of predictable quality where the crystal is of a portion of the core RNA polymerase with rifampicin without undue experimentation.

CLAIM REJECTIONS 35 USC § 103

38. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

39. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

40. Claims 27-29 and 31-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Darst et al. (US006225076B1) in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983). This rejection is maintained with respect to claims 27-29, as recited in the previous office action Paper No. 15, mailed January 29, 2003. It is noted that the instant rejection has been extended to claims 31-47.

Response to Applicants' Arguments

41. Applicants argue that the structure of Rif-RNAP is functionally related to the process of claim 27 because the structure is necessary to implement the claim method. Applicants' argument have been fully considered and found to be unpersuasive. It is acknowledged that the structure of Rif-RNAP is related to the method of claims 27-29 due to the data being used as a component of the active steps of the said method. However, the said crystal structure data do not impart functionality to said method, but merely stored (Table 2) for 3-dimensional modeling. Therefore, the limitation of the atomic coordinates in Table 2 of claims 27-29 is regarded as being directed to nonfunctional descriptive material.

42. It is re-iterated that Darst et al. discloses "a method of identifying an agent that inhibits bacterial growth comprising:

43. (a) selecting a potential agent by performing rational drug design with the set of atomic coordinates in Table 3, wherein said selecting is performed in conjunction with computer modeling;

44. (b) contacting the potential agent with a bacterial culture; and

45. (c) measuring the growth of the bacterial culture under conditions in which the bacterial culture grows in the absence of the agent; wherein a potential agent is identified as an agent

that inhibits bacterial growth when there is a decrease in the growth of the bacterial culture in the presence of the agent relative to in its absence.

46. (d) contacting the agent with a eukaryotic cell; and

47. (e) measuring the amount of proliferation of the eukaryotic cell under conditions in which the eukaryotic cell proliferates in the absence of the agent; wherein an agent is identified as an agent for inhibiting bacterial growth when there is no change in the proliferation of the eukaryotic cell in the presence of the agent relative to in its absence; and wherein the agent identified inhibits bacterial growth but not eukaryotic proliferation." (Claims 7 and 8), as in instant claims 27-29 and 33-47. It is noted that the specific limitation of atomic coordinates in Table 2 of claim 27 and dependent claims; and the further limiting requirements of claims 33-47 are directed to nonfunctional descriptive material as discussed below.

48. Further, once the agent is identified, the said agent may be synthesized de novo (column 22, lines 28-29), as in instant claims 31 and 32.

49. Even though the method disclosed by Darst et al. does not specify that the atomic coordinates be derived from rifampicin bound to the core RNA polymerase (Rif-RNAP), the specific limitations of atomic coordinates of rifampicin bound to the core RNA polymerase in this instant case do not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.

50. In re Gulack defines nonfunctional descriptive material, as when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in term of patentability. Also, the MPEP indicates that

descriptive material that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition (MPEP § 2106 (IV)(B)(b)).

51. Darst et al. discloses, "[i]nitially, compounds known to bind bacterial RNA polymerase, for example rifampicin which binds to the .beta. subunit, can be systematically modified by computer modeling programs until one or more promising potential analogs are identified" (Column 22, lines 1-8). This is achieved by fitting of potential modulators such as rifampicin to the RNA polymerase by 3-D modeling based on crystal structure data thus suggests the crystal structure of rifampicin-bound RNA polymerase (column 21, lines 40-44).

52. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Darst et al. for a method of identifying a compound that is predicted to inhibit bacterial growth. Darst et al. also teaches compounds such as rifampicin which bind to RNA polymerase could be model to identify analogs (Column 22, lines 1-8) and "[a] potential inhibitor (e.g., a candidate drug) would be expected to interfere with bacterial growth" (Column 24, lines 52-55). Further, the critical limitation of atomic coordinates of rifampicin bound to the core RNA polymerase is regarded as nonfunctional descriptive material as defined by In re Gulack. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Darst et al. for identifying a compound that is predicted to inhibit bacterial growth.

CONCLUSION

53. NO CLAIM IS ALLOWED.

54. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

55. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

56. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

57. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
8/19/03

ARDIN H. MARSCHEL
PRIMARY EXAMINER